II. REMARKS

Preliminary Remarks:

Claims 21-39 are re-numbered as claims 20-38, respectively, in response to the notice of non-compliant amendment mailed June 29, 2005. The following remarks refer to the re-numbered claims only.

Claims 2, 3, 30, 32, 33, and 34 are amended, and claim 29 is canceled. No fee for additional claims is believed to be due.

Claims 2, 3, 30, 32, 33, and 34 are amended to specify that the claimed method comprises identifying anti-human gp39 antibodies that are non-agonistic of a human T-cell activation response, as described, for example, on page 12, lines 26-28, of the application.

Claim 2 is further amended to specify that the claimed method comprises the steps of:

- assaying to identify anti-human gp39 antibodies that compete for binding to human gp39 with murine antibody 24-31, produced by hybridoma cells assigned ATCC accession no. HB-11712;
- identifying anti-human gp39 antibodies that inhibit the interaction of human gp39 with CD40, compete with murine antibody 24-31 for binding to human gp39, and are non-agonistic of a human T-cell activation response selected from the group consisting of T-cell proliferation, the production of interleukin 2 (IL-2), the production of interleukin-4 (IL-4) and the production of interferon γ (IFN-γ); and
- administering a therapeutically effective amount of said anti-human gp39 antibodies that inhibit the interaction of human gp39 with CD40, compete with murine antibody 24-31 for binding to human gp39, and are non-agonistic of said human T-cell activation response;

support for which is found, for example, at page 13, lines 1-6, of the application.

Claims 2 and 3 are also amended by deleting the word "substantially," so that anti-human gp39 antibodies of the claimed invention are described as being "non-agonistic of a human T-cell activation response," support for which is found, for example, at page 12, lines 26-31, of the application.

Claim 18 is amended to be directed to the improved method of claim 17, wherein the anti-gp39 antibodies that are administered are chimeric antibodies having light and heavy

chain variable regions of an antibody of an Old World monkey, and constant regions of human antibodies, support for which is found, for example, at page 9, lines 15-18.

Patentability Remarks:

35 U.S.C. §112, First Paragraph – written description

Claims 2, 3, 5, 16-30, and 32-38 were rejected under 35 U.S.C. § 112, first paragraph, because the specification allegedly does not provide adequate written description of anti-gp39 antibodies that are "substantially" non-agonistic of a T-cell activation response. In response, claims 2 and 3 are amended by deleting the word "substantially." Withdrawal of the rejection of the claims under 35 U.S.C. § 112, first paragraph, for lack of written description of anti-gp39 antibodies that are "substantially" non-agonistic of a T-cell activation response, is respectfully requested.

35 U.S.C. §112, First Paragraph – enablement by the specification

Claims 23-29 were also rejected under 35 U.S.C. § 112, first paragraph, because the specification allegedly does not describe antibody 24-31 in terms that enable one to practice the claimed invention. The official action requires that the record state that all restrictions to the availability to the public of the deposited cell line that produces antibody 24-31 will be irrevocably removed upon the granting of the patent. Filed herewith is a declaration executed by the undersigned, as the authorized representative of Biogen Idec, Inc., the successor of the assignee of the application, which states that all restrictions to the availability to the public of the deposited cell line that produces antibody 24-31 will be irrevocably removed upon the granting of the patent. Withdrawal of the rejection of the claims under 35 U.S.C. § 112, first paragraph, for non-enablement of the claimed method is therefore respectfully requested.

35 U.S.C. §112, Second Paragraph

Claims 2, 3, 5, 16-30, and 32-38 were rejected under 35 U.S.C. § 112, second paragraph, because the meaning of the word "substantially" as used in the claims was considered to be indefinite. As noted above, the word "substantially" has been deleted from claims 2 and 3, and withdrawal of the rejection of the claims under 35 U.S.C. § 112, second paragraph, for alleged indefiniteness the word "substantially" is respectfully requested.

Claim 18 was also rejected under 35 U.S.C. § 112, second paragraph, because it described included the trademarked term "primatized®." Claim 18 is amended by replacing references to "primatized®" antibodies with description of the antibodies as chimeric antibodies having light and heavy chain variable regions of an antibody of an Old World monkey, and constant regions of human antibodies, support for which is found at page 9, lines 15-18. Withdrawal of the rejection of the claims under 35 U.S.C. § 112, second paragraph, for use of a trademarked term is respectfully requested.

35 U.S.C. §103(a)

Claims 2, 3, 5, 16-30 and 32-38 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable in view of Black et al. (U.S. Patent No. 6,001,358), considered in combination with Schrader et al. (U.S. Patent No. 5,627,052), Burkly et al. (US2002/0028202 A1), and Wilson et al. (U.S. Patent No. 6,372,208 B1).

The applicants respectfully traverse the rejection of the claims under 35 U.S.C. § 103(a) as allegedly being obvious in view of Black et al., Schrader et al., Burkly et al., and Wilson et al.. The currently amended claims of the present application are directed to the disclosed improved method of treating an autoimmune disease or disorder that expressly includes the steps of:

(1) obtaining anti-human gp39 antibodies;

(2) assaying to identify anti-human gp39 antibodies that inhibit the interaction of human gp39 with CD40;

(3) assaying to identify anti-human gp39 antibodies that compete for binding to human gp39 with murine antibody 24-31, produced by hybridoma cells assigned ATCC accession no. HB-11712;

(4) assaying to identify anti-human gp39 antibodies that are non-agonistic of a human T-cell activation response selected from the group consisting of T-cell proliferation, the production of interleukin 2 (IL-2), the production of interleukin-4 (IL-4) and the production of interferon γ (IFN-γ);

(5) identifying anti-human gp39 antibodies that inhibit the interaction of human gp39 with CD40, compete with murine antibody 24-31 for binding to human gp39, and are non-agonistic of said human T-cell activation response; and

(6) administering a therapeutically effective amount of said anti-human gp39 antibodies that inhibit the interaction of human gp39 with CD40, compete with murine antibody 24-31 for binding to human gp39, and are substantially non-agonistic of said human T-cell activation response.

Prior to the present invention, it was not known that anti-human gp39 antibodies could be obtained that compete for binding to human gp39 with murine antibody 24-31, inhibit the interaction of human gp39 with CD40, and are non-agonistic of a human T-cell activation response selected from the group consisting of T-cell proliferation, IL-2 production, IL-4 production, and IFN-γ.

Black et al., the primary reference cited in the statement of the rejection, described anti-human gp39 antibodies that compete for binding to human gp39 with murine antibody 24-31. However, as discussed in the previous response, Black et al. did not describe or suggest a method for obtaining anti-gp39 antibodies that includes steps of assaying for and identifying such anti-human gp39 antibodies that are determined to be non-agonistic of a human T-cell activation response selected from the group consisting of T-cell proliferation, the production of IL-2, the production of IL-4, and the production of IFN- γ.

As described in the application, one of ordinary skill in the art at the time of filing would have recognized that human $CD4^+$ T cells that have been pre-treated with CD3 ligand to induce expression of gp39 are strongly stimulated to proliferate and produce IFN-γ by the anti-human gp39 antibody huSC8 (see Blair et al., J. Exp. Med., 191(4):651-660, esp. Fig. 1A on p. 653 and Fig. 3 on p. 655, copy enclosed). The application further demonstrates that human $CD4^+$ T cells that have been pre-treated with CD3 ligand to induce expression of CD40L are also stimulated by TRAP-1, a murine antibody anti-human gp39 antibody, to proliferate and produce IFN-γ as well as IL-2 and IL-4. Blotta et al. taught that triggering of CD40L on T cells had been previously shown to function as a co-stimulus for $CD4^+$ T cell proliferation (p. 3133, right column), and showed that human $CD4^+$ T cells that have been pre-treated with CD3 and CD28 ligands are stimulated by the anti-human gp39 antibody M90 to produce high levels of IL-4 (J. Immunology, 1996, 156:3133-40, copy enclosed). Moreover, the data in Table 5 of Black et al. shows that in two separate experiments, treatment of hu-PBL-scid mice with the anti-human gp39 antibody 24-31 resulted in a greater percentage of the mice showing an anti-tetanus T cell proliferative response than treatment

with PBS (see col. 24). In view of the foregoing, one of ordinary skill in the art at the time of filing would reasonably have expected anti-human gp39 antibodies to be agonistic of human T-cell proliferation and the production of one or more of IL-2, IL-4, and IFN-γ.

The secondary references also fail to describe or suggest the claimed method for obtaining anti-gp39 antibodies that includes steps of assaying for and identifying such anti-human gp39 antibodies that are determined to be non-agonistic of a human T-cell activation response selected from the group consisting of T-cell proliferation, the production of IL-2, the production of IL-4, and the production of IFN-γ.

Schrader et al. described a method for screening a population of antibody producing cells to identify a cell that produces antibodies having a selected activity.

Burkly et al. described making antibodies that bind to the gamma chain of a cytokine receptor and inhibit a cytokine response (for example, see paragraph 0017).

Wilson et al. taught that the proliferation of murine T cells that are re-stimulated by an antigen in vivo in the presence of the anti-murine gp39 antibody MR1 is inhibited by about 90% in lung and by about 80% in liver, compared to the level of T cell proliferation in control mice that were not injected with the MR1 antibodies (see col. 21).

In view of the strong anti-proliferative effect of MR1 antibodies on murine T cells described by Wilson et al., in contrast to the known ability of anti-human gp39 antibodies to stimulate T cell proliferation, one of ordinary skill in the art at the time of filing would reasonably have suspected that the epitope on murine gp39 that is bound by the anti-murine gp39 antibody MR1 either does not correspond structurally to the epitopes bound by the anti-human gp39 antibodies huSC8, TRAP1, and 24-31, or that murine and human T cells respond differently to anti-gp39 antibodies. Schrader et al. and Burkly et al. also would have suggested to one of ordinary skill in the art a method of screening to find anti-human gp39 antibodies that bind to epitopes on human gp39 that are different from the epitopes bound by known anti-human gp39 antibodies. Nothing in the Schrader et al., Burkly et al., or Wilson et al. references would have suggested to one of ordinary skill in the art the claimed method of assaying for, identifying, and administering anti-human gp39 antibodies that inhibit the interaction of human gp39 with CD40, compete for binding to human gp39 with murine antibody 24-31, and are non-agonistic of a human T-cell activation response selected from the group consisting of T-cell proliferation, the production of IL-2, the production of IL-4, and

the production of IFN-γ. Accordingly, the claimed invention would not have been obvious in view of Black et al. in combination with Schrader et al., Burkly et al., and Wilson et al., and withdrawal of the rejection of the claims under 35 U.S.C. § 103(a) is respectfully requested.

Conclusion

All rejections having been addressed, it is respectfully submitted that the present application is in condition for allowance and a Notice to that effect is earnestly solicited. If any points remain in issue, which the examiner feels may be best resolved through a personal or telephone interview, he is kindly requested to contact the undersigned attorney at the telephone number listed below.

Respectfully submitted,
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